REMARKS

Claims 1-41 are pending in the subject application. By this Amendment, applicant has canceled claims 1-9 and 14-41 without prejudice or disclaimer to applicant's right to pursue the subject matter of these claims in the future. Applicant has also amended claims 10-13 and added new claim 42.

Support for amended claim 10 may be found in the specification, *inter alia*, on page 32, line 29 to page 34, line 24; page 40, line 29 to page 41, line 4; and page 43, lines 10-20. Support for amended claim 12 may be found in the specification, *inter alia*, on page 24, line 15; page 32, line 29 to page 34, line 24; page 36, lines 4-8; and page 43, lines 17-20. Support for new claim 42 may be found in the specification, *inter alia*, at page 36, lines 4-8. Applicant maintains that claims 10-13 as amended and new claim 42 do not raise any issue of new matter. Accordingly, applicant requests that this Amendment be entered and considered. Upon entry of this Amendment, claims 10-13, as amended, and new claim 42 will be pending and under examination.

Sequence Rules Compliance

The Examiner objected to the application as allegedly failing to comply with the sequence rules as set forth in 37 C.F.R. §§1.821-1.825. The Examiner stated that sequences in the specification must be identified by corresponding SEQ ID NOs.

In response, applicant has herein amended the specification to recite SEQ ID NOs after each sequence found in the specification. Accordingly, applicant maintains that the specification as now amended complies with the requirements of 37 C.F.R. §§1.821-1.825, and respectfully requests that the Examiner reconsider and withdraw this ground of objection.

Objection to the Brief Description of the Drawings

The Examiner objected to the Brief Description of the Drawings as allegedly failing to comply with the requirements set forth in 37 C.F.R. §1.84 which requires a specific heading, i.e. "Brief Description of the Drawings", and that each figure be described by a number followed by a letter descriptor if applicable.

In response, applicant has amended the specification to recite "Brief Description of the Drawings" and each figure to be described by proper numbers and letter descriptors. Accordingly, applicant maintains that the specification as amended complies with the requirements of 37 C.F.R. §1.84 and respectfully requests that the Examiner reconsider and withdraw this ground of objection.

Rejections Under 35 U.S.C. §112, Second Paragraph

The Examiner rejected claims 10-13 under 35 U.S.C. §112, second paragraph, as allegedly indefinite for failing to distinctly point out and claim the subject matter which applicant regards as the invention. Specifically, the Examiner alleged that the claims are indefinite because they depend on a withdrawn claim and the structure of the estrogen receptor as claimed is not clear.

In response, but without conceding the correctness of the Examiner's ground of rejection, applicant notes that claims 10 and 12, have been amended to recite "a plasma membrane receptor ER-X" rather than "the receptor of claim 1." Claims 10 and 12 have been amended to further define the plasma membrane receptor ER-X by reciting that "the plasma membrane receptor ER-X has a molecular weight of 62-63kDa and is obtainable by (i) contacting a neocortex tissue lysate from an estrogen receptor-α knockout mouse with a murine monoclonal antibody raised against estrogen receptor alpha (ER-α) designated 6F11 under conditions which permit the formation of a complex between the 6F11 antibody and ER-

X; (ii) capturing the complex between the 6F11 antibody and ER-X with an anti-mouse IgG-coated polystyrene magnetizable bead; (iii) precipitating the complex; and (iv) separating ER-X from the complex based upon molecular size."

Applicant maintains that one of skill in the art would understand that the murine monoclonal antibody designated F611 refers to the antibody commercially available from Vector Laboratories, Inc. As is stated in the 6F11 antibody datasheet from Vector Laboratories,Inc, the 6F11 is raised against the full length alpha form of estrogen receptor molecule. Applicant attaches herewith as **Exhibit A**, a copy of the 6F11 antibody datasheet from the Vector Laboratories, Inc, for the Examiner's review. Accordingly, applicant maintains that, as amended, claims 10-13 comply with the requirements of 35 U.S.C. §112, second paragraph and respectfully requests that the Examiner reconsider and withdraw this ground of rejection.

Rejections Under 35 U.S.C. §112, First Paragraph, Enablement

The Examiner rejected claims 10-13 under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which is not described in the specification in such a way as to enable one skilled in the relevant art to make and/or use the invention. Specifically, the Examiner alleged that the plasma membrane receptor ER-X is not sufficiently defined by structural and functional limitations recited in claim 1, from which claims 10 and 12 depend. The Examiner also indicated on page 4 of the April 5, 2007 Office Action that, while the specification is enabling for a method for determining whether an agent is an agonist or an antagonist of the plasma membrane associated estrogen receptor (ER-X), the specification does not reasonably provide enablement for a receptor defined by steps a-c of claim 1.

In response, but without conceding the correctness of the Examiner's ground of rejection, applicant notes that claims 10 and 12 have been

amended to recite "a plasma membrane receptor ER-X" further defined by reciting that "the plasma membrane receptor ER-X has a molecular weight of 62-63kDa and is obtainable by (i) contacting a neocortex tissue lysate from an estrogen receptor-α knockout mouse with a murine monoclonal antibody raised against estrogen receptor alpha (ER-α) designated 6F11 under conditions which permit the formation of a complex between the 6F11 antibody and ER-X; (ii) capturing the complex between the 6F11 antibody and ER-X with an anti-mouse IgG-coated polystyrene magnetizable bead; (iii) precipitating the complex; and (iv) separating ER-X from the complex based upon molecular size."

Applicant maintains that the isolation of the plasma membrane receptor ER-X is described in the subject application on page 32, line 8 to page 34, line 24. Applicant notes that the detection process utilized neocortical tissue lysates obtained from mice deficient for the ER-α gene (ERKO) so as to avoid isolating any other estrogen receptor. See page 31, lines 4 to 8 of the specification. Applicant further notes that while the neocortex samples obtained from wildtype mice expressed both the 67kDa ER-α band and the 62-63kDa ER-X band, the neocortex tissue samples from the ERKO mice contained only the 62-63kDa band, reaffirming that the receptor detected was ER-X, rather than ER-α, which has a molecular weight of 67kDa, or ER-β, which has a molecular weight of 60kDa.

Applicant also maintains that the plasma membrane receptor ER-X is defined in the subject specification by specific immunoprecipitation, western blotting, light and electron microscopy, ligand binding and molecular weight. Specifically, ER-X is defined in the subject specification *inter alia* at page 40, line 33 to page 41, line 4, as having a molecular weight of 62-63 kDa; at page 42, lines 15-27; and page 24, line 15, as having a selective ligand of 17α-estradiol in a concentration of at least 0.1pM and less than 100pM; at page 47, lines 17-23, as being maximally expressed at ~P7-10 in both the neocortex and the uterus; and at page 43, line 25 to page 44, line 14, as having an activating effect on the MAPK pathway, evidenced by increased ERK1/2

phosphorylation.

Accordingly, applicant maintains that the specification provides more than adequate enablement for methods for determining whether an agent is an agonist or antagonist of the plasma membrane receptor ER-X as now recited in claims 10 and 12.

Applicant maintains that claims 10 and 12 as amended, and claims 11 and 13 dependent therefrom, respectively, and new claim 42 satisfy the enablement requirement of 35 U.S.C. §112, first paragraph, and respectfully request that the Examiner reconsider and withdraw this ground of rejection.

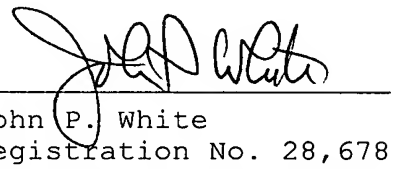
Conclusion

In view of the remarks and arguments made hereinabove, applicant respectfully submits that the grounds of objection and rejection set forth in the April 5, 2007 Office Action have been overcome. Applicant therefore respectfully requests that the Examiner reconsider and withdraw these grounds of rejection, and further request allowance of all claims pending in the subject application, namely, claims 10-13, as amended, and new claim 42.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicant's undersigned attorney invites the Examiner to telephone him at the number provided below.

No fee, other than the $225.00 fee for a two-month extension of time, is deemed necessary in connection with the filing of this Amendment. Accordingly, a check for the $225.00 is enclosed. However, if any fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,



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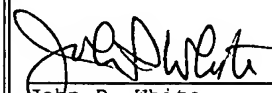

9/5/07

John P. White Date
Reg. No. 28,678

EXHIBIT A

VECTOR LABORATORIES

Antibody to **Estrogen Receptor** Cat. No. **VP-E613**

Product Specifications

Description:
Estrogen Receptor mouse monoclonal antibody

Immunoglobulin class: IgG1

Clone: 6F11

Immunogen: Prokaryotic recombinant protein representing the full length alpha form of the estrogen receptor molecule.

Epitope: Within first 184 amino acids of estrogen receptor molecule.

Presentation:
1 ml liquid tissue culture supernatant containing 15mM sodium azide.

Species cross-reactivity: Human, monkey, and rabbit.

Storage Conditions:
Keep unopened vial at 2 - 8 °C for 1 year. Once opened it is recommended that the stock solution be aliquoted and quick frozen and stored at -20 °C. Do not repeatedly freeze/thaw.

Applications:

Immunohistochemistry

Paraffin sections:	Antigen unmasking recommended.
Frozen sections:	Zamboni's fixative 10 minutes at 25 °C.
Working Dilution*:	1:40 - 1:80 for 1 hr. at 25 °C
Positive Control:	Uterus. Nuclear staining pattern.

Western blotting

Working Dilution*:	1:50 - 1:100
Positive Controls:	MCF-7 cell line

* Recommended dilutions using VECTASTAIN® *Elite*® ABC Kits.

Functional Aspects:
Estrogen receptor (ER) is expressed in a variety of d i fferent tissues but is found most prominently in the female reproductive tract. A large amount of research has focused on the differential expression of ER in human breast cancer. This antibody will help detect the presence of ER in tissues and cell lines.

Selected References

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VP-E613 is recommended FOR PROFESSIONAL AND RESEARCH USE ONLY.

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Filed: September 19, 2003
Exhibit A